

AMENDMENTS TO THE DRAWINGS

The attached sheets of drawings replace the original sheets including Figures 11 and 12.
In Figure 11 and Figure 12, the previously defects have been corrected.

Attachment: Replacement sheets (2)

REMARKS

After entry of this amendment, claims 1-11, 15-25 and 27-32 are pending, of which claims 1-10, 16, 24-25, and 29-30 are withdrawn. Claims 12-14 have been cancelled without prejudice or disclaimer. New claims 31 and 32 have been added and find support *inter alia* in the original claims. Further support for the newly added claims is found in the specification at page 26, lines 11-16 and page 40, lines 37-43. Claims have been amended without prejudice or disclaimer to delete the non-elected subject matter, to better comply with U.S. practice, and to address the various points made in the Office Action. The amended claims find support *inter alia* in the original claims. Claims 1 and 11 find further support in the specification at page 26, lines 11-16 and page 40, lines 37-43. No new matter has been added.

Withdrawn method claims have also been amended to require all the limitations of the product claims. Support is found *inter alia* in the original claims. No new matter has been added. In the event that the product claims are found allowable, rejoinder of the withdrawn method claims is respectfully requested. MPEP § 821.04(b).

Applicants submit herewith Replacement Sheets containing Figures 11 and 12 that correspond to Figures 11 and 12 as originally filed, respectively. The only amendments made to Figures 11 and 12 are the presentation format of each column, therefore Annotated Sheets Showing Changes are not provided. Support for the amendments made to Figures 11 and 12 is found *inter alia* in the original figures as filed. No new matter has been added. Entry of the Replacement Sheets of drawings is respectfully requested.

Drawings

The Examiner objects to Figures 11 and 12 for containing portions that are illegible. In response, Figures 11 and 12 have been amended to change the presentation format of each column.

In view of the present amendments, it is believed that this objection is rendered moot.

Claim Objections

The Examiner objects to various points in the claims. In view of the present claim amendments, the objections are believed to be rendered moot.

Claim Rejection – 35 USC § 112, second paragraph

The Examiner rejects claims 18 and 19 under 35 U.S.C. § 112, second paragraph, for indefiniteness. In view of the present amendments, it is believed that this rejection is rendered moot. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejection – 35 USC § 112, first paragraph

Claims 11, 15, 17-23, 27 and 28 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement and lacking an enabling disclosure. Applicants respectfully disagree. However, to expedite prosecution, the claims have been amended without prejudice and disclaimer to recite the claimed nucleic acid with more specificity. It is respectfully submitted that the more commensurate scope of the claims as amended overcomes the rejection.

Written Description Rejection

The Examiner alleges that the specification does not provide an adequate written description for the claimed genus of molecules. To address this concern, Applicants have amended the claims without prejudice or disclaimer to recite the lysophosphatidic acid acyltransferase (LPAAT) coding nucleic acid with more specificity. For example, claim 11 has been amended to recite the LPAAT coding nucleic acid based on the nucleotide sequence of SEQ ID NO: 16 or the encoding polypeptide sequence of SEQ ID NO: 17, and variants having at least 80% identity to SEQ ID NO: 16 or SEQ ID NO: 17.

As amended, the claims relate to subject matter clearly described and enabled. For example, claim 11 now requires that the nucleic acid sequence is one with (1) a particular structure (e.g., one with a specified nucleotide sequence, or one having 80% sequence identity therewith), and (2) a specific enzymatic activity (e.g., LPAAT activity). Thus, only nucleic acid molecules which meet the claimed structure and have the specified enzymatic activity are within the scope of the present claims.

Furthermore, it is respectfully submitted that the specification provides a representative number of species within the genus now claimed. This is a proper means of complying with the written description requirement. As stated in *Eli Lilly and Co.*, “[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs.” 43

USPQ2d 1398, 1406 (Fed. Cir. 1997). In addition to SEQ ID NO: 16, the specification further provides a second LPAAT coding sequence from *Mortierella alpina* and LPAAT coding sequences from other species such as *Thraustochytrium*, *Physcomitrella patens*, and *Shewanella hanedai*. Among those LPAAT coding sequences, the second LPAAT coding sequence from *Mortierella alpina* is 100% identical to SEQ ID NO: 16 in the overlapping region. Thus, the specification provides at least two species that are within the genus recited in the amended claim, and allows the skilled artisan to readily envision further species having the claimed level of identity. Because these two sequences clearly constitute a representative number of species within the claimed genus of sequences, it is respectfully submitted that the claims as amended satisfy the written description requirement.

Separate consideration is respectfully requested as to claims 31 and 32 which recite that the LPAAT coding sequence has at least 95% sequence identity with the sequence of SEQ ID NO: 16, or encodes a polypeptide sequence having at least 95% sequence identity with the sequence of SEQ ID NO: 17.

For at least the above reasons, it is submitted that the amended claims have overcome the written description rejection. Reconsideration and withdrawal of the rejection is respectfully requested.

Enablement Rejection

The Examiner alleges that the specification does not provide any evidence that SEQ ID NO: 17, and the derivatives thereof, functions as an LPAAT or would have the claimed function in any non-human organism. The Examiner further asserts that none of the examples indicate that SEQ ID NO: 16 or any other derivative was used for transformation and the fatty acid composition of the transformed organism was analyzed. Applicants respectfully traverse.

As provided in Example 16, at pages 96-98 of the specification, a *Mortierella* LPAAT (MaLPAAT) was transformed into yeast and the LPAAT enzymatic activity was confirmed by the feeding experiments with the transformed yeast as demonstrated in Figure 23-26. Note that the MaLPAAT coding sequence used in Example 16 corresponds to the sequence of SEQ ID NO: 16. Reconsideration is respectfully requested, since the asserted function has been demonstrated.

The Examiner further argues that the function of derivatives identified by sequence homology and the identification of related sequences encoding enzymes involved in modifying fatty acids is unpredictable, citing literature references. For instance, the Examiner asserts that Broun *et al.* (Science, 1998, 282: 1315-1317, hereinafter "Broun") taught that a change in four amino acids converted a desaturase to a hydroxylase gene. In response, Applicants submit that the present claims are fully enabled and that Broun actually supports enablement.

The changes in the amino acids described in Broun were in the conserved amino acid residues identified when the sequences of six desaturases and two hydroxylases were compared. Seven amino acid residues were found to be strictly conserved in the desaturases. See Broun at page 1315, paragraph bridging center and right columns. The experiment described in Broun resulted in "a major increase in desaturase activity and a decrease in hydroxylase activity upon introduction of the seven desaturase-equivalent residues into LFAH12," a hydroxylase. Broun at page 1316, left column, lines 26-32. Furthermore, modification of a single one of these seven conserved amino acids was found not to change the activity of the enzyme when compared to the wild type. Broun at page 1316, right column, lines 1-4. Thus, Broun actually teaches that a modification even in the conserved amino acid residues does not necessarily affect enzyme activity. The four amino acid residues (four of the seven conserved residues) noted by the Examiner were found adjacent to histidine residues that were identified as essential to catalysis. Broun at page 1316, right column, last paragraph. Changes in all four of these specific amino acid residues adjacent to the active site did affect desaturase activity. Broun concluded that because of the substantial effect of the four residues that abut the active site histidines, the difference between desaturase and hydroxylase was influenced by changes in active site geometry. Broun at page 1317, left column, lines 22-27. Thus, the Examiner's statements regarding identification of sequences by similarity to other known desaturases is inapposite to the teaching in Broun. Rather Broun teaches which amino acids substitutions can and cannot be made which will affect enzyme activity from the identification of conserved residues based on sequence comparisons.

One of skill in the art when aligning various LPAAT enzymes such as those disclosed in the instant specification would readily be able to identify conserved residues and motifs, and, from the teachings of Broun and the specification, know where (and where not) to effect

substitutions. Method of generating such mutations or substitutions, for example, site-directed mutagenesis and PCR-mediated mutagenesis, are standard techniques readily available and known to those skilled in the art. See Broun and specification at page 48, lines 29-34. Furthermore, the screening and selecting of a nucleic acid with the specified sequence homology while maintaining the desired enzymatic property is routine to those skilled in the art, as evidenced by Broun, and is described in the specification.

Moreover, the specification provides detailed guidance on how to isolate and clone LPAAT coding nucleic acid from various species (Example 13), how to determine the enzymatic activity of the polypeptide encoded by the isolated nucleic acid in straightforward assays (Example 16), how to generate transgenic organisms such as plants (Example 18), and how to analyze the transgenic plants (Example 19). It is submitted that determining the enzymatic activity is routine and not undue experimentation. This is further evidenced by Broun as well. As stated in *Ex parte Jackson*, under the applicable law, the test for “undue experimentation” is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. *Ex parte Jackson*, 217 USPQ 804, 807 (1982). On the facts of this case, the detailed guidance provided in the specification and the routine nature of the screening for activity outweighs the unpredictability concerns noted by the Examiner.

Accordingly, in view of the detailed description, guidance, working examples, state of the art, and high level of skill, the specification enables the full scope of the claims without undue experimentation. On these facts, a proper analysis of the relevant factors supports enablement. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Reconsideration and withdrawal of the enablement rejection is respectfully requested.

Separate consideration is respectfully requested as to claims 31 and 32 which recite that the LPAAT coding sequence has at least 95% sequence identity with the sequence of SEQ ID NO: 16, or encodes a polypeptide sequence having at least 95% sequence identity with the sequence of SEQ ID NO: 17.

For these reasons and in light of the amendments, reconsideration and withdrawal of this rejection is respectfully requested.

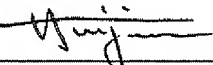
CONCLUSION

In view of the above remarks and further in view of the above amendments, Applicants respectfully request withdrawal of the rejections and allowance of the claims.

Applicants reserve all rights to pursue the non-elected claims and subject matter in one or more divisional applications, if necessary.

Applicants are submitting their response within the three-month response period. No fee is believed due. However, if a fee is due, please charge our Deposit Account No. 03-2775, under Order No. 13478-00002-US from which the undersigned is authorized to draw.

Respectfully submitted,

By 

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